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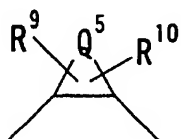
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[続葉有]

(54) Title: ETHYLENEDIAMINE DERIVATIVES

(54) 発明の名称: エチレンジアミン誘導体

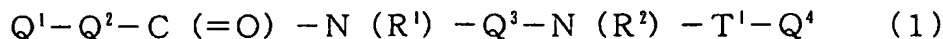
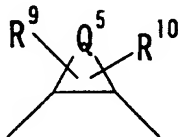


(2)

(57) Abstract: Compounds of the general formula (1): Q¹-Q²-C(=O)-N(R¹)-Q³-N(R²)-T¹-Q⁴; and drugs which contain the compounds and are efficacious for thrombosis and embolism. In said formula, wherein R¹ and R² are each H or the like; Q¹ is an aromatic ring, a heterocycle, or the like; Q² is a single bond, an aromatic ring, a heterocycle, or the like; Q³ is a group of the general formula (2), or the like; Q⁴ is an aromatic ring, a heterocycle, or the like; and T¹ is -CO- or -SO₂-.

(57) 要約:

本発明は式 (1)

(式中、R¹およびR²はHなど; Q¹は芳香環、複素環など; Q²は単結合、芳香環、複素環など; Q³はなど; Q⁴は芳香環、複素環など; T¹は-CO-または-SO₂を示す)

で表される化合物およびこれを含有する血栓症、塞栓症に有効な医薬に関する。

Derwent WPI records

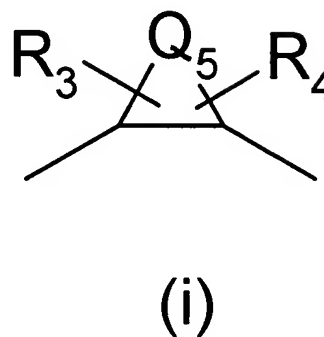
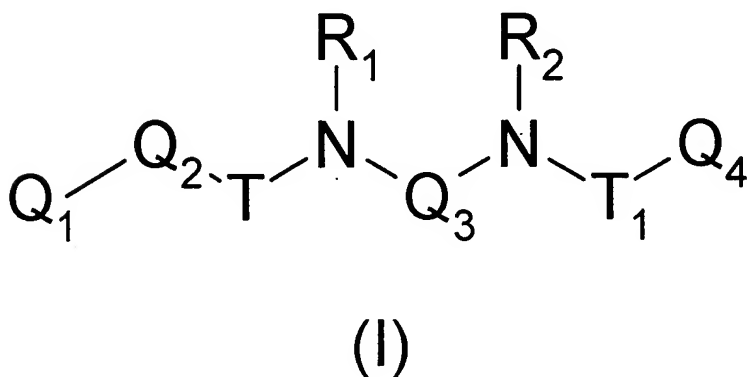
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L7 3 S L6

L7 ANSWER 1 OF 3 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-256264 [25] WPIX Full-text
CR 2003-247888 [24]; 2003-312743 [30]
TI New diamine compounds are activated blood factor X inhibitors used for
treating e.g. cerebral or myocardial infarction and angina.
PA (DAUC) DAIICHI PHARM CO LTD
PI WO 2003000657 A1 20030103 (200325)* JA 788 C07D209-42 <--
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ZW
PRAI JP 2001-398708 20011228; JP 2001-187105 20010620;
JP 2001-243046 20010809; JP 2001-311808 20011009
TECH UPTX: 20030410



TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) Are prepared e.g.
by reacting an amine of formula (IV) with an acid of formula (V).

AB WO2003000657 A UPAB: 20030513

NOVELTY - Diamine compounds (I) are new.

DETAILED DESCRIPTION - Diamine compounds of formula (I) and their salts, solvates and N-oxides are new. R1, R2 = H, OH, alkyl or O-alkyl; Q1 = 5-6C carbocyclyl, 5-7 membered heterocyclyl or bi- or tri-cyclic carbocyclyl or heterocyclyl (all optionally unsaturated and optionally substituted);

Q2 = a bond, or divalent 5-6C carbocyclyl, 5-7 membered heterocyclyl or bi- or tricyclic carbocyclyl or heterocyclyl (all optionally unsaturated and optionally substituted); Q3 = a group of formula (i);

Q5 = 1-8C alkylene, 2-8C alkenylene or (CH2)mCH2ACH2(CH2)n; m, n = 0-3;

A = O, N, S, SO, SO2, NH, ONH, NHH, SNH, SONH or SO2NH; R3, R4 = H, OH, alkyl (optionally substituted by CN, NH2, NHA, NAA, acyl, acylamino, O-alkyl, OH, COOH, COO-alkyl, NHCOOA, N-alkenylcarbamoyl, N-alkenyl-N-alkyl-carbamoyl, CONHO-alkyl, CON(A)OA, SO2A, CONH2, OCONH2, OCONHA, OCONAA, OCOHet, COHet, Ar1, NHSO2alkyl, NHSO2Ar, CONHSO2alkyl, CONHSO2Ar or optionally

substituted CONHA or CONAA), alkenyl, alkynyl, halo, acyl, optionally substituted acylamino, O-alkyl, COOH, COO-alkyl, NHACOOA, NHACOOH, CONH2, CONHA, CONAA, N-alkenylcarbamoyl, N-alkenyl-N-alkyl-carbamoyl, CONHO-alkyl, CON(A)OA, CON(A)3, SO2A, COHet, Ar1, NHSO2alkyl, NHSO2Ar, CONHSO2alkyl, CONHSO2Ar, oxo, OCONH2, aralkoxy, O-alkyl-COOH, acyloxy, SO2Ar, SO2-alkyl-COO-alkyl, SO2-alkyl-COOH, acyl (substituted by COO-alkyl, OH, O-alkyl, halo, COOH, NH2, acyloxy, NH-alkyl, N(alkyl)2, SO2alkyl or optionally substituted CON(alkyl)2, COO-alkyl-O-alkyl or acyloxyalkylsulfonyl, SO2-alkyl-OH, SO2O-alkyl, SO2Het or optionally substituted SO2CON(alkyl)2, or R3 + R4 = 1-5C alkylene, 2-5C alkenylene, 1-5C alkyleneoxy or carbonyldioxy; Het = optionally substituted 3-6C heterocyclyl; Ar1 = aryl or heteroaryl;

Ar = aryl;

Q4 = Ar1, arylalkenyl, arylalkynyl, heteroarylalkenyl or optionally unsaturated bi- or tricyclic carbocyclyl or heterocyclyl (all optionally substituted);

T = CO or CS;

T1 = CO, SO2, COCONR11, CSCONR11, COCSNR11, CSCSNR11, COA1NR12, CONH, CSNH, CONHNH, COA2CO, COA3CONH, COC(=NORa)NRb, CS(=NORa)NRbCON=N, CSN=N or CS;

R11, R12, Rb = H, OH, alkyl or O-alkyl; A1 = optionally substituted 1-5C alkylene; A2 = bond or A1, and

Ra = H, alkyl or alkanoyl.

ACTIVITY - Cerebroprotective; Cardiant; Antianginal; Respiratory; Anticoagulant; Thrombolytic; Vasotropic; Antiinflammatory.

MECHANISM OF ACTION - Factor X Inhibitor. In tests on rats, administration of N1-(4-chlorophenyl)-N2-((1S,2R,4S)-4-((dimethylamino)carbonyl)-2-((5-methyl-4,5,6,7-tetrahydrothiazolo(5,4-c)pyridin-2-yl)carbonyl)amino)cyclohexyl)ethanediamide (Ia) (10 mg/kg orally) reduced blood FXa levels over 4 hours by 62-96%.

USE - As activated blood factor X inhibitors for treating and preventing e.g. cerebral infarction, cerebral embolism, myocardial infarction, angina, pulmonary, embolism, Buerger's disease, deep vein thrombosis, disseminated intravascular coagulation, thrombosis following artificial flap/hip replacement or during external circulation, reocclusion, systemic inflammatory reaction syndrome, multiple organ failure or blood coagulation during blood collection. Dwg.0/0

ABEX

UPTX: 20030410

ADMINISTRATION - Administration of (I) is 0.1-200 (preferably 0.5-100) mg/kg/day orally or by injection.

EXAMPLE - 1-Hydroxybenzotriazole monohydrate (71 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloric acid (100 mg) were added to N-((1Rasterisk,2Sasterisk)-2-aminocyclopropyl)-5-chloroindole-2-carboxamide (108 mg) and lithium 5-methyl-4,5,6,7-tetrahydrothiazolo(5,4-c)pyridine-2-carboxylate (124 mg) in dimethylformamide (3 ml) and the mixture was stirred at room temperature for 8 hours. Work-up including silica gel chromatography (methylene chloride:methanol 10:1) gave 72 mg of N-((1Rasterisk,2Sasterisk)-2-((5-chloroindol-2-yl)carbonyl)amino)cyclopropyl)-5-methyl-4,5,6,7-tetrahydrothiazolo(5,4-c)pyridine-2-carboxamide hydrochloride.